

CLAIMS

We Claim:

5 1. A variant type I interferon protein exhibiting improved solubility relative to a wild type interferon protein selected from the group consisting of SEQ ID NOs: 1-18.

10 2. A variant type 1 interferon protein according to claim 1 wherein said variant type 1 interferon protein maintains at least one biological activity selected from the group consisting of immunomodulatory, antiviral, and antineoplastic activities.

15 3. A variant type I interferon according to claim 1 wherein said variant interferon differs from a naturally occurring interferon of SEQ ID NOs: 1-18 by at least one substitution of a solvent-exposed hydrophobic residue.

20 4. A variant type I interferon according to claim 1 wherein said variant interferon is incapable of dimer formation.

25 5. A variant type I interferon according to claim 1 wherein said variant interferon has reduced immunogenicity as compared to a wild type interferon of SEQ ID NOS: 1-18.

30 6. A variant interferon according to claim 1 wherein said variant interferon is derived from an interferon-alpha selected from the group consisting of SEQ ID NOs: 1-14.

35 7. A variant interferon according to claim 1 wherein said variant interferon is derived from the interferon-beta of SEQ ID NO: 15.

40 8. A variant interferon according to claim 1 wherein said variant interferon is derived from the interferon-kappa of SEQ ID NO: 16.

30 9. A variant interferon according to claim 6 comprising modifications selected from at least one of the following positions: 16, 27, 30, 89, 100, 110, 111, 117, 128, and 161, wherein said modifications are substitution mutations selected from the group consisting of alanine, arginine, aspartic acid, asparagine, glutamic acid, glutamine, glycine, histidine, serine, threonine, and lysine.

40 10. A variant interferon according to claim 7 comprising modifications selected from at least one of the following positions: 5, 8, 15, 22, 28, 30, 32, 36, 47, 92, 111, 116, 120, 130, 148, and 155, wherein said modifications to residues 5, 8, 15, 47, 111, 116, and 120 are substitution mutations selected from the group consisting of alanine, arginine, aspartic acid, asparagine, glutamic acid, glutamine, glycine, histidine, and lysine, and said modifications to residues 22,

28, 30, 32, 36, 92, 130, 148, and 155 are selected from the group including alanine, arginine, aspartic acid, asparagine, glutamic acid, glutamine, glycine, histidine, serine, threonine and lysine.

- 5 11. A variant type I interferon according to claim 10 comprising at least one modification selected
 from the group consisting of: L5Q, F8E, W22E, L28Q, Y30H, L32A, L47K, Y92Q, F111N,
 L116D, L116E, L120D, L120R, L130R, V148A, and Y155S.
- 10 12. A variant type I interferon according to claim 11 comprising at least one modification selected
 from the group consisting of: L5Q, F8E, L47K, F111N, L116E, and L120R.
13. A variant interferon according to claim 1 comprising SEQ ID NO: 19.
14. A variant type I interferon according to claim 1 comprising SEQ ID NO: 20.
- 15 15. A variant type I interferon according to claim 1 comprising SEQ ID NO: 21.
16. A variant type I interferon according to claim 1 comprising SEQ ID NO: 22.
- 20 17. A variant type I interferon according to claim 1 comprising SEQ ID NO: 23.
18. A variant type I interferon according to claim 1 comprising SEQ ID NO: 24.
- 25 19. A variant type I interferon according to claim 1 comprising SEQ ID NO: 25.
- 20 20. A variant type I interferon according to claim 8 comprising at least one modification at the
 following positions: 1, 5, 8, 15, 18, 28, 30, 33, 37, 46, 48, 52, 65, 68, 76, 79, 89, 97, 112, 115,
 120, 127, 133, 151, 161, 168, and 171, wherein said modifications are substitution mutations
 selected from the group consisting of alanine, arginine, aspartic acid, asparagine, glutamic
 acid, glutamine, glycine, histidine, serine, threonine, and lysine.
- 30 21. A variant type I interferon according to claim 20 comprising at least one modification selected
 from the group consisting of: L5Q, V8N, W15R, F28Q, F28S, V30R, I37N, Y48Q, M52N,
 M52Q, F76S, Y78A, I89T, Y97D, M112T, M115G, L133Q, V161A, C166A, Y168S, and
 Y171T.
- 35 22. A variant type I interferon according to claim 21 comprising SEQ ID NO:26.
23. A variant type I interferon according to claim 20 comprising SEQ ID NO:27.
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24. A variant type I interferon according to claim 20 comprising SEQ ID NO:28.
25. A variant type I interferon according to claim 20 comprising SEQ ID NO:29.
- 5 26. A variant type I interferon according to claim 20 comprising SEQ ID NO: 30.
27. A variant type I interferon according to claim 3 wherein said interferon is interferon-beta and comprises at least one modification selected from a modification at a position selected from the group consisting of: 1, 2, 3, 4, 5, 6, 8, 9, 12, 16, 42, 43, 46, 47, 48, 49, 51, 93, 96, 97, 100, 101,
10 104, 113, 116, 117, 120, 121, and 124.
28. A variant type I interferon according to claim 27 comprising at least one modification at a position selected from the group consisting of: L5A, L5D, L5E, L5K, L5N, L5Q, L5R, L5S, L5T, F8A, F8D, F8E, F8K, F8N, F8Q, F8R, F8S, S12E, S12K, S12Q, S12R, E43K, E43R, E104R, E104K, E104H, E104Q, E104A, R113D, R113E, R113Q, R113A, L116D, L116E, L116N, L116Q, L116R, and M117R.
29. A recombinant nucleic acid encoding a variant interferon selected from claim 1.
- 15 30. An expression vector comprising the nucleic acid of claim 29.
31. A host cell comprising the recombinant nucleic acid of claim 29.
32. A host cell comprising the expression vector of claim 30.
- 25 33. A method of producing a variant interferon comprising culturing the host cell of claim 32 under conditions suitable for expression of said nucleic acid.
- 30 34. A method according to claim 33 further comprising recovering said variant interferon.
- 35 35. A pharmaceutical composition comprising a variant type I interferon of claim 1 and a pharmaceutical carrier.
36. A method of treating an interferon-responsive condition in a patient needing said treatment comprising administering the pharmaceutical composition of claim 35.
37. A method of inhibiting interferon dimer formation comprising contacting a variant interferon of claim 1 with a wild type interferon of SEQ ID NOs: 1-18.